

# The C5 variant of the butyrylcholinesterase tetramer includes a noncovalently bound 60 kDa lamellipodin fragment

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## Abstract

© 2017 by the authors. Licensee MDPI. Humans with the C5 genetic variant of butyrylcholinesterase (BChE) have 30–200% higher plasma BChE activity, low body weight, and shorter duration of action of the muscle relaxant succinylcholine. The C5 variant has an extra, slow-moving band of BChE activity on native polyacrylamide gel electrophoresis. This band is about 60 kDa larger than wild-type BChE. Umbilical cord BChE in 100% of newborn babies has a C5-like band. Our goal was to identify the unknown, 60 kDa protein in C5. Both wild-type and C5 BChE are under the genetic control of two independent loci, the BCHE gene on Chr 3q26.1 and the RAPH1 (lamellipodin) gene on Chr 2q33. Wild-type BChE tetramers are assembled around a 3 kDa polyproline peptide from lamellipodin. Western blot of boiled C5 and cord BChE showed a positive response with an antibody to the C-terminus of lamellipodin. The C-terminal exon of lamellipodin is about 60 kDa including an N-terminal polyproline. We propose that the unknown protein in C5 and cord BChE is encoded by the last exon of the RAPH1 gene. In 90% of the population, the 60 kDa fragment is shortened to 3 kDa during maturation to adulthood, leaving only 10% of adults with C5 BChE.

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## Keywords

Butyrylcholinesterase, C5 phenotype, Lamellipodin, RAPH1, Tetramer

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